LETTERS TO THE EDITOR

Successful treatment of recalcitrant condyloma with topical cidofovir

EDITOR,—Despite the high prevalence of condylomata acuminata, their treatment remains unsatisfactory for both patients and physicians. Epidemiological studies estimated the prevalence of genital warts between 1–31% with a peak occurring in young adults.[1] As a consequence, the economic burden of human papillomavirus (HPV) infection in the United States is estimated to exceed $8.5 billion per year.[2] Current treatments rely on the ablation of warts (cryotherapy, laser vaporisation, electrodissection, or trichloroacetic acid) or the interruption of cell division (podophylox, intralesional or systemic interferon, and 5-fluorouracil). Recently, imiquimod has been successfully used as a topical immune response modifier for the treatment of external anogenital warts.[3] However, there remains a substantial number of patients who fail to respond to traditional and newer drugs. We report on such a patient with recalcitrant condylomata acuminata on the glans and shaft of the penis who was successfully treated using the novel virustatic cidofovir as a 1.5% gel.

A 48 year old man with a 2½ year history of condylomata acuminata had received laser treatment, podophylox, and imiquimod. The patient's history was remarkable for diabetes mellitus. He presented with numerous, flesh coloured, flat topped papules in a circular manner on the outer preputium and the glans, whereas some lesions in the coronary sulcus had a more verruciform appearance (fig 1). On histological analysis, the typical picture of acanthosis, papillomatosis, and numerous koilocytes was seen. Papillomavirus typing revealed HPV-43 by nested PCR using consensus primers.[4]

Cidofovir was evaluated in the indicator patient at 1.5% cidofovir in a viscous gel (propylene glycol, parabene). Initially, the patient was treated on an outpatient basis with two applications of cidofovir gel per week to the respective lesions without any side effects. Thereafter, the patient was instructed to apply the gel three times a week by self application. At week 6 the patient presented with small erosions surrounded by a marked erythema on all treated sites (fig 1). The lesions were painful. Condylomata were still present in the coronary sulcus. At this point treatment was stopped and antiseptic treatment was given with betadine solution once daily. Seven weeks later (week 13) all lesions had completely healed (fig 1). Neither scarring nor dysaesthesia were noted. No recurrence has occurred since. Cidofovir, 1-[(S)-3-hydroxy-2-(phosphono-methoxy)-propyl]cytosine, is a member of a new class of antiviral agents (phosphonylmethylether nucleotide analogues).[5] It shows potent in vitro activity against a broad spectrum of herpesviruses, including human cytomegalovirus (CMV), HSV-1 and HSV-2, and adenovirus.[6] Recent in vitro and in vivo studies have demonstrated activity against papillomavirus and poxvirus.[6 7]

Cidofovir is a nucleotide analogue of deoxycytidine monophosphate (dCMP). Analogous to the metabolism of dCMP to dCTP, cidofovir is converted to the active cidofovir diphosphate that inhibits viral DNA polymerases.[8] The uptake of cidofovir into cells is slow, but the intracellular half life of the various metabolites is between 6 and 87 hours, thus allowing infrequent dosing.[8] Compared with the general mechanism of activation of ganciclovir, which requires phosphorylation by the virus encoded UL97 gene, cidofovir does not depend on viral infection for its phosphorylation and can therefore prime cells to an antiviral state (prophylaxis).

The metabolism of cidofovir is negligible, since the majority (>80%) is recovered unchanged in the urine. The principal systemic toxicity (nephrotoxicity) can be avoided by topical application.

This initial case report suggests that topical cidofovir may represent a valuable addition to the armamentarium of hard to treat condyloma. However, a careful evaluation of the dose and frequency of cidofovir application is warranted.

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Figure 1 Condylomata acuminata with some lesions in the coronary sulcus having a more verruciform appearance.

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Bladder carcinoma presenting to genitourinary medicine departments

EDITOR,—Large numbers of patients are seen in departments of genitourinary medicine with symptoms suggesting infection or inflammation of the genitourinary tract. Although bladder neoplasms typically cause painless haematuria, in a subgroup of patients they cause other urinary symptoms that may produce diagnostic confusion. We identified five patients who were referred to the genitourinary medicine service, and who were found to have bladder carcinoma (see table 1). Four of the patients presented to the genitourinary medicine department at High Wycombe (5500 new attendances per annum) between 1991 and 1998; the fifth patient presented to the Oxford genitourinary medicine department (9000 new attendances per annum) in 1997. None of the patients had an occupational history that placed them at higher risk for bladder cancer.

Men with bladder carcinoma typically present in later life (median age 69 years), but the condition may occur at younger ages.[1] A subgroup of patients develop frequency, urgency, and dysuria—symptoms usually associated with bladder infection.[2] Rarely, penile and perineal pain mimicking prostatitis may be a presenting feature, as in patients 3 and 4, who have been described in more detail elsewhere.[3]

Non-specific urethritis (NSU) is diagnosed commonly in genitourinary medicine clinics in men of all ages. In this series, patient 2 was referred with presumed NSU, and patient 4 had attended previously with a diagnosis of NSU, 2 years before the bladder cancer was diagnosed (at that time there were 5–10 white cells/high power field (×1000) on a urethral smear, and a chlamydia ELISA test and cultures for *Neisseria gonorrhoeae* were negative; no haematuria was detected). Both patients were subsequently noted to have neoplastic infiltration in the bladder neck area and prostatic urethra.

In all five cases a degree of persistent microscopic haematuria was noted at presentation; in patient 4 this was never greater than a trace on dipstick testing. Patient 1 reported intermittent painless macroscopic haematuria at presentation; he was referred by his general practitioner with suspected